In The Matter Of:

In Re: Viagra Products Liability Litigation

DANIEL A. SHAMES
March 13, 2009

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SHAMES, DANIEL A. - Vol. 1

UNITED STATES DISTRICT COURT

DISTRICT OF MINNESOTA

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In re

Viagra Products Liability Litigation,

MDL Docket No. 1724

This Document Relates to All Actions

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March 13, 2009

10:55 a.m.

Deposition of DANIEL A. SHAMES, taken by Plaintiffs, pursuant to Notice, at the offices of Kaye Scholer LLP, 425 Park Avenue, New York, New York, before ERIC J. FINZ and ANITA SHEMIN, Shorthand Reporters and Notaries Public within and for the State of New York.

APPEARANCES:
BEFORE:
JOHN W. BORG, ESQ.
Special Master

THE MILLER LAW FIRM, LLC
Attorneys for Plaintiffs
Two Bala Plaza
Bala Cynwyd, Pennsylvania 19004
BY: CHRISTOPHER A. GOMEZ, ESQ.

KAYE SCHOLER LLP
Attorneys for Pfizer
425 Park Avenue
New York, New York 10022

BY: LORI B. LESKIN, ESQ.
-and-
MARK D. SPATZ, ESQ.

ALSO PRESENT:
CHRISTINE HOGAN, Kay Scholer LLP

DANIEL A. SHAMES

DANIEL A. SHAMES,
having been first duly sworn by the Notary Public (Eric J. Finz), was examined and testified as follows:

EXAMINATION BY
MR. GOMEZ:

Q. Good morning, Dr. Shames.
A. Yes.
Q. Did I pronounce that correctly?
A. Yes.
Q. We met earlier. My name is Chris Gomez, I'm here to take your deposition today. From what I understand, this is your first time ever giving a deposition?
A. That's correct.
Q. Before we begin, let me go over a few things with you. I'm going to be asking the questions, you'll be providing me the answers. I'm usually the culprit, but we can't talk over each other so the court reporter can take down an accurate record. Feel free to tell me if I'm doing that, because I'm the one that usually does it.
A. Okay.

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Q. Any time you don't understand my question, you'll tell me?
A. Yes.
Q. So if you do answer my question, I'm going to assume you answer it truthfully and fully. Is that fair?
A. That's fair.
Q. If you need a break at any time, as Judge Borg indicated, please tell me, and we'll accommodate you.
A. Um-hum.
Q. If you could just state your full name and address for the record.
A. Daniel A. Shames. In New York it's 180 West End Avenue, Apartment 27-B, New York, New York.
Q. And are you a medical doctor?
A. Yes.
Q. What's your specialty?
A. Urology.
Q. And do you currently treat patients?
A. No, I do not.
Q. I have seen some indications that

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you have a urology practice in South Carolina; is that correct?
A. I had a urology practice in South Carolina, that is correct.
Q. When did you stop being associated with that practice?
A. In 1996.
Q. Okay. Have you treated patients in the urology field since 1996?
A. I briefly treated patients early on during the period when I started at FDA in a clinic, in a teaching, I was an associate professor at Georgetown. And I was in a clinic with the residents and performed some teaching services and treated patients with the residents. I did a clinic. Only one half afternoon a week.
Q. Okay. Doctor, I'm going to mark now as Exhibit 1, Shames 1, what's called the notice of your videotape deposition, which is not being videotaped.
(Shames Exhibit 1 for identification, notice of videotape deposition.)

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Q. I'll just pass that to you.

MR. GOMEZ: Lori, do you need a copy?

MS. LESKIN: I don't have a copy with me.

Q. Doctor, have you seen that document before?

A. Yes, I have. I have seen this document before.

Q. I just want to point your attention to the, just go to the back, I believe it's the third page from the back, there is a page entitled "attachment A."

Do you see that?

A. Yeah, I see that.

Q. When you received that document and reviewed it, did you have a chance to go through all the things on there to determine if you had any responsive documents?

A. Yes, I did.

Q. And just for the record, I've been provided with a pile of documents here that you reviewed in preparing your report as well as your deposition. Is that fair?

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A. That is correct.

Q. Now, I'm going to go through these in a moment -- strike that.

I'm going to go through these right now, then at the end I'll ask you if there is anything else that you reviewed. But I was provided, just for the record, a CD-ROM entitled Pfizer Viagra expert report of Daniel L. Shames, M.D. It's been represented to me that on this CD-ROM are all the medical literature and the materials you reviewed that is referenced in your report, I believe it's in appendix B or appendix 2.

A. Yes. I personally have not seen that CD, but it represents, I've been told it represents all the material that I reviewed. The materials that you have there are the materials that I marked up. There is some redundancy, because I think those materials are also on the CD-ROM.

MS. LESKIN: Just for the record, what's on there are the things that are cited in his expert report or cited on that attachment to his expert report as

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material he relied upon.

MR. GOMEZ: You mean the appendix and whatever's cited within the expert report?

MS. LESKIN: Exactly.

Q. Doctor, I was also provided with an updated curriculum vitae. We will go over this in more detail in a moment, but I just wanted to point that out for the record.

A. Okay.

Q. And some deposition transcripts that you reviewed. And you've reviewed the deposition transcripts of Gregory Gribko?

A. It may be -- I may have looked at it. I didn't review that one in extreme detail. There were others that I've reviewed in more detail.

Q. Okay. And there was also a deposition transcript of Stephen Watt. Do you remember reviewing that?

A. I was given that, but I didn't review that in detail.

Q. Okay. And finally deposition of Michael Witt, M.D.

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A. That also I was given but I didn't review it in detail. The other ones, you have other ones that I have reviewed in more detail.

Q. Did you review the deposition transcript of Dr. Cheryl Bloom?

A. Yes.

Q. And moving on to this other pile of documents that was provided to me. This one is a folder which has written on it regulatory -- "reg. HX labelling Viagra."

That's safe to say that's regulatory history Viagra?

A. Yes.

Q. And you reviewed these documents?

A. Yes.

Q. I'm not going to ask you questions about all of these documents, I'm going to move on to a few in a moment. I want to identify some of these for the record.

Here's a folder titled "Dr. Shames's emails." Did you print these out?

A. No.

Q. I've looked through the emails, and I might be incorrect, but I only see that you had email correspondence with Ms. Leskin.
A. Yes. There was one exception, I believe I did have a correspondence from, one correspondence from Ms. Hogan regarding a web site or something. But virtually all of them were from Ms. Leskin.
Q. I stand corrected, I did see an email from -- who is Ms. Hogan?
A. Ms. Hogan is the associate, I believe.
Q. Okay.
A. And also I think I have a couple of emails from Todd Porter, who is the legal assistant or whatever you call it.
Q. Did you search your own computers for the emails?
A. Yes. That's how --
Q. Did you print them out?
A. I had -- no, I did not.
Q. Okay. Why not?
A. Because I was having some trouble -- this was a few days ago, I was

having trouble with my printer, so I contacted Mr. Spatz and said I'm having some trouble with my computer -- my printer. Which is a home printer. And can I just forward these to you.
Q. Okay. So what you did is you looked at all your emails on your computer, rather than printing them out yourself you forwarded them to Kaye Scholer, Ms. Leskin's office?
A. I have a search option, which brings up all the emails. And I went through the emails, and each one individually I forwarded.
Q. And you did that within the last few days?
A. Yes.
Q. Okay.
MR. GOMEZ: Off the record.
(Discussion off the record.)
Q. Doctor, we've talked about the emails, okay. That's one folder that was provided to me. Another manila is entitled "citizen, I think I can read your handwriting,

citizen petitioner's." Let me hand this to you. Whatever it in black ink under there, what that says.
A. It says citizen petitions and summaries. I must say that, you know, this is my own system and may have been using it for something else and then I -- this says original NDA vision summary, which I don't think is still in this folder. But this is, these were primarily the citizens petitions and, you know, the two citizen petitions.
Q. The ones in 1998 and 2005?
A. Right.
MS. LESKIN: Just make sure you don't talk over him.
MR. GOMEZ: I'm really bad at that. Lori, feel free to let me know.
Q. Okay, we've identified that.
Another manila entitled "Bloom," deposit, I assume that means deposition. And then ER.
A. Expert report.
Q. Okay.. That's another folder.
Another one is, if you could just

read that for me.
MS. LESKIN: He just wants you to read what's on top.
Q. I just want you to read what's on the tab there.
A. What is on the tab here has no relationship to what's in the -- this has to do with my check. I took this from somewhere else, and there is no relationship between what's on there.
Q. I do it all the time. No problem.
But within this are some documents, just for the record, when I open it up is a, one entitled "feasibility assessment of a case control study to determine whether Sildenafil Viagra is an independent risk factor for NAION."
Did you print these out yourself or were these documents provided to you?
A. I believe that they were provided --
MR. GOMEZ: I'm sorry, let's go off.
(Discussion off the record.)

Q. Doctor, I'm looking at some documents that were provided to me before the deposition that are responsive to attachment A of the notice of deposition. And I was just asking about this folder of documents, I think my specific question was, did you print these out yourself or were they provided to you by Ms. Leskin, counsel for Pfizer?

A. I would have to look at the documents. Most of the documents I got were provided to me, but I did, I believe, look up some papers by myself and print them out. So I would have to look up -- I would have to look at the whole folder to see which it was.

Q. Let me pass this to you. If you don't mind me walking around. You stay seated, doctor. I just want to hand this to you.

And within this folder I've put in front of you is a copy of what we'll refer to later that's in your report, the McGwin study. Do you see that?

A. Yes, I do.

Q. If you could just read for me the

notes here, what does that say?

A. "Selection bias."

Q. What do you mean by that?

A. I mean that in my view, this was a case cohort study, and in my view there was some bias in the selection of the cases. They did not exactly match the controls because they were taking PDE5 inhibitors, which in my view meant they had perhaps more advanced cardiovascular disease than the controls. That's what I meant by that.

Q. That's a criticism, your criticism of this study?

A. That's correct.

Q. And down at the bottom there is some other handwriting. Can you just read that for me.

A. I'm not sure I can read it completely. But it does say aged matched. It's the same concept as this.

Q. Okay. I'm sorry, finish your answer.

A. Often when I'm reviewing a document, I will just scribble things down to

keep a thought in my head and then later when I go back I may not be able to read it. But that's the concept of what was in there.

Q. So people like me can ask you questions about it. I'm not going to go through every single one of your handwritings at all. Or we'd be here until tomorrow.

MR. BORG: Your profession does have a bit of a reputation about how it writes.

Q. Doctor, another folder here is entitled CFRs, et cetera. CFR, Code of Federal Regulations. And I believe you listed, we'll go over those in a while when we go over your report, but you did list some specific CFR regulations that you reviewed?

A. That is correct.

Q. Would those be contained in this? Do you need to see it to make sure?

A. Yes.

Q. Here you go.

A. These were materials that generally dealt with CFRs. And CFR -- and information in the title CFR that might be

related to my report or other issues here.

Q. We'll go over those, I might have some specific questions later on when we go over your report. So if you just want to hand that back to me so I can keep these in order.

And I have another manila folder here with some documents inside, with for lack of a better word, I'll call them sticky notes, and your writing on them. And written on the folder is, I think I can read this, early eye labelling stuff. I can't read this, but I'll attempt it, Wiley Chambers?

A. Wiley Chambers, yes.

Q. Who is that?

A. Wilily Chambers is one of the senior ophthalmologists at the FDA who was involved in the early interactions between FDA and Pfizer regarding eye issues. In fact, he's still involved in those issues. So this has to do mostly, I believe, with the early labelling interactions and review of material that was in the original NDA, and some of the materials that followed with early labelling issues in the first six months or so after the

drug was approved.
Q. And underneath Wiley Chambers is ERG, and then another word I can't read. On this one, for the record, I point that out to you. Can you read that for me?
A. ERG is electroretinogram.
Q. Okay.
A. And I don't know what other word is.
Q. Fair enough.
Doctor, I might come back to these and ask you some questions.
A. Okay.
Q. But a few more folders here. This one was provided to me, and the first page that I open to is your, it looks like your first invoice in this case dated December 30, 2008. When were you first contacted regarding reviewing this case?
A. I believe it was in December. I believe it was in December of last year, 2008.
Q. Your invoice begins --
THE WITNESS: November?
MS. LESKIN: For the record, I

think it's two pages. There may be two separate invoices there.
MR. GOMEZ: Right. I'm asking about the first one.
Q. I'm not trying to trick you up, doctor. Because I'm looking at the document and you're not. Your first entry on here is dated 9th November, review of Viagra documents. So you would have been contacted before that?
A. Yes. I believe there is actually an email, and I don't remember the date, but there is an email I believe in which Ms. Leskin first contacts me, I think.
Q. Okay. And you charge $500 an hour?
A. That is correct.
Q. And that's for reviewing documents and any deposition time?
A. That is correct.
Q. And your first invoice, dated from 29th of November to the 30th of December of 2008; correct? And the total was $36,125. Does that sound right?

A. That sounds right, yes.
Q. That's what the document says. I'll represent that to you. $36,125.
A. That is correct.
Q. And then attached to this is page 2, is a January 31, 2009 invoice. And you spent, I'm not good at the math, but the total for the month of January was $5,250; correct?
A. That is correct.
Q. Did you prepare a February invoice?
A. I think I did, but it may have been -- I think I have -- we were supposed to, what I've already been paid for, I do have a February invoice. I can get it.
Q. From what I understand it, is this deposition was originally scheduled for sometime in early February. Do you remember that, being told that?
A. I think I recall something about this being scheduled in early February, yes, February 4th or 5th or something.
Q. We're now at March 13th. Did you do any work on this case in February?

A. Actually, I may not have done any work on this case in February. I may not have had a February invoice.
Q. Okay. If you could just check your files, if there is a February invoice, provide it.
A. I may not have had a February invoice.
Q. Okay. I'll keep this one to the side because we are going to talk about your report in a few minutes, and I'll have a few questions about that.
But also within this folder is a copy of the notice of videotaped deposition.
A document dated June 24, 2005, with United States Senate letterhead on it. I might have a few questions about that. It looks like it was from Senator Grassley?
A. Yes.
Q. And you reviewed this in preparing your report?
A. Yes, I did.
Q. Also within here is the Supreme Court of the United States opinion in Wyeth

versus Levin. Did you read this?
A. Yes, I did.
Q. Are you going to rely on anything in this, did you glean anything from this, with your report, obviously this came down after your report was authored, but anything you'd like to --
A. I don't think it's critical to anything. I believe that it was important for me to understand somewhat what was in that report. I'm not sure I can say that I totally understood the -- I can say that I did not totally understand all the legal ramifications.
Q. And also within this folder is a document entitled "Federal Register," from Wednesday, January 16, 2008.
Do you remember reviewing that?
A. Yes. That document has to do with some perhaps changing of the rules regarding, surrounding issues regarding CBEs, change being effected, regulations. I read it as a background, background information.
Q. Briefly, what are some of the

changes being discussed in this document regarding CBEs?
A. I believe that this document actually states that it's not really a change, but it's putting into -- putting down in the regulations what has been the practice previously of the FDA, essentially that a CBE is not the routine way that labelling changes are created. That's done primarily through a supplement, prior approval supplement. So that the FDA can have an opportunity to review information that the company may have and review wording, make sure that the wording is properly associated with the information, with the data.
And that's what that document talks about.
Q. Okay. And moving on to another folder, written in I believe it's your handwriting, and underlined twice, it says "my issues."
What does that mean?
A. Well, I think, I'm not sure that what's in there has anything to do with my

issues.
Q. Okay.
A. My issues were simply as I went through expert testimony and discussions, these were issues that I felt I had to do, you know, particular research about. I mean, brushing up on the regulations or at one time Dr. Bloom's deposition may have been in there. Things that I personally thought were important issues in this case.
Q. Okay. And within this --
A. What's in there now may have nothing to do with what I at one time thought were my issues. Just I happened to put it into that folder. But I'm not sure what's in there right now.
Q. I don't want to get bogged down going through it. I might just put this aside. I have a question about this document, but I can ask it in context later. I'm just going to move on.
Finally is a folder entitled "Pfizer NDA."
A. Revision summary.

Q. It looks like fee/S vision summary. I thought that was an L. And summary from FDA.
A. Right. I don't know exactly what's in that. But certainly the vision summary is the portion of the -- excuse me, of the NDA that was submitted by Pfizer in which they review all the vision issues, all the information related to vision issues.
Q. Let me pass this over to you. This is a, what's entitled "Sildenafil visual summary."
A. Yes.
Q. A few questions about this document. First of all, if you could just, there is some handwriting. Can you read that for me?
A. "Pfizer affirmatively looked at vision problems in NDA. No NAION plus look at NDA review." This is a note to myself because I noted one of the issues was whether Pfizer was, I think maybe this was in Dr.. Bloom's expert report, but I had the impression that Dr. Bloom did not the think that Pfizer was

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aggressively looking at the vision issues.

And I was looking to see, looking at this material and other material to see if they had adequately studied certain vision issues. So at one time I may have -- I had issues, and I put perhaps the supporting documents under the issues. Something like that.

Q. And that you would have had -- strike that.

What this is is a response to some of the opinions in Dr. Bloom's report?

A. Correct.

Q. Okay. And we'll go through your report.

A. Okay.

Q. But we don't need to waste time right now. I would like to keep this together.

Doctor, I have asked you some questions about your curriculum vitae, some of your background. On here it says under professional experience, October 2008 to present, that you're the president of the

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Daniel A. Shames Consulting, Inc.?

A. Yes.

Q. What do you do?

A. I consult with primarily pharmaceutical companies on issues related to their interactions with FDA, communications and interactions with FDA. And also regarding their planning of clinical trials, their development of particular drugs. The clinical trial issues, drug evaluation issues. Kind of scientific issues. And also regulatory issues related to FDA interactions. Or proposed FDA interactions.

Q. Has Pfizer retained you in that capacity?

A. No, they have not.

Q. What other pharmaceutical companies?

A. I'm not sure I can say that. Most of them have confidentiality agreements.

Q. I'm not asking you to say what you're doing, but can you name the companies?

A. Some of the companies actually don't want me to say that I'm working for the

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company.

Q. I don't want to get you in trouble. Let me ask this way --

A. About fifteen pharmaceutical companies from very large pharmaceutical companies, large multinational companies, to very small companies where there are one or two people.

Q. Okay. And also you mentioned on here that litigation departments of large law firms.

A. Yes.

Q. Are you consulting as an expert witness in any other cases besides this litigation, as we sit here today?

A. Yes.

Q. And which litigations would that be?

MS. LESKIN: I just want to caution and see if we can get some foundation to make sure that he's not -- if he's a consulting expert and not a testifying expert, that is privileged information. And so I think we need to

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make a distinction to where he's supposed to be a testifying expert as opposed to a consulting expert. Because that's protected information.

MR. BORG: Will you carve those up?

MR. GOMEZ: Absolutely. Let me rephrase the question.

Q. Have you been retained by any litigation law firms to be a testifying expert on behalf of a pharmaceutical company?

A. Yes.

Q. Okay. Which pharmaceutical companies were those? And I'm asking you about testifying expert, not consulting expert.

A. Right. Merck, other counsel for Merck, which is --

Q. And what litigation is that?

A. This is --

Q. What drug does that involve?

A. Fosamex, which is Aledronate, and the issue is osteonecrosis of the jaw.

Q. Have you been, obviously this is

your first deposition.

What others, besides Merck?

A. The other one is Roche, which is Accutane. And irritable -- excuse me, inflammatory bowel disease.

Q. Let me just back up to Merck. Any other drugs besides Fosamex?

A. No.

Q. That you reviewed for Merck?

A. No.

Q. Okay. We talked about Roche. Any others?

A. There may be one or two others that I'm not at the point where I know I'm going to be a testifying. So I'm not sure if I'm just consulting.

Q. Well, if you're not sure, that's good enough. I don't want you to have to answer that.

A. Okay.

Q. Have you been contacted by any plaintiffs to be an expert in any pharmaceutical litigations?

A. I have not been contacted by any

plaintiffs.

Q. Okay. Going back to your CV, I'm going to go work from the past to the present, rather than from the present to the past. We are under the section entitled "professional experience."

You were in the United States Army Medical Corps?

A. Yes, I was.

Q. From 1977 to 1979?

A. That is correct.

Q. And you practiced urology at Fort Jackson, South Carolina?

A. That's correct.

Q. And I think I read in your report that you were honorably discharged at that time?

A. That is correct.

Q. And then you went to work for, what did you do after that, there seems to be a six year gap here between 1979 and 1985. Maybe it's just out of order. I see 1979 to 1996, that's where you were working for Urology Consultants?

A. Yes, I founded a urology practice, a private practice in South Carolina. And ultimately hired two other urologists, and the practice was still going when I left in 1996. But I was continually in practice from the time I left the Army until I left South Carolina.

Q. So in 1996, is that when you went to work for the FDA?

A. That is correct.

Q. Okay. Tell me about that. What was your first position at the FDA?

A. I was a medical officer at the FDA, which is an individual that primarily reviews the material related to drug development, in various stages, all stages of drug development. Early drug development, at the time when a sponsor, a company wants to put the drug for the first time into a human being, on to later trials, phase II trials, which primarily were dose finding. Phase III trials, where we're testing the efficacy of the drug. And during this time there is usually a lot of interaction between myself

and the company.

And if the drug is marketed, there is continual evaluation of safety, et cetera. That's what a primary medical officer does.

Q. I'll ask you some more questions about that when we get into your report.

But you were the deputy director of DRUP?

A. Yes, I was.

Q. And what is, for a layperson, what is DRUP?

A. It's the division of reproductive and urologic products.

Q. And you were there from 2000 to 2001?

A. In that position, correct.

Q. Okay. And then from 2001 to 2006, you were the director of the division of reproductive and urologic drug products, DRUPP?

A. It's the same division.

Q. Same division?

A. Yes. I was the director.

Q. The sole director at this point?

A. The sole --
Q. I see you had shared responsibility with that before; correct?
A. Absolutely, yes.
Q. And then from 2007 to 2008, you were the director of the division of gastroenterology and in borne error products?
A. That is correct.
Q. What was your role in that position?
A. Well, I was the director, meaning I was in charge of the scientific and administrative and regulatory functioning of that division. I became the director of that division because I was actually in a higher position in the office, a higher supervisory position. And that particular division was having some difficulty and the senior management at the office of new drugs asked me to take that division over and help it out. Straighten it out and run it for a while. I ran it for about a year, eight months.
Q. Okay. And then you went on to be deputy director office of drug evaluation 3?

A. That is correct.
Q. Okay. And along with that title is the ODE 3, what's that?
A. Office of drug evaluation is ODE.
Q.. And then it says "/CDER." Can you, for the record, what's that?
A. Center for drug evaluation and research.
Q. Okay. And you were in that position from 2006 to 2008 when you left the Food and Drug Administration; right?
A. That is correct.
Q. Going to a little bit -- doctor, are you board certified?
A. Yes, I am.
Q. In what specialty?
A. Urology.
Q. You did your undergrad at Brandeis University?
A. Brandeis University, yes.
Q. 1963 to 1967?
A. That is correct.
Q. Georgetown Medical School?
A. That is correct.

Q. And then you went on to do your residency at the University of Pennsylvania?
A. That is correct.
Q. In Philadelphia?
A. That is correct.
Q. 1973 to 1974, National Institute of Health, postdoctoral fellow in renal research?
A. That is correct.
Q. It says here you published research in peer reviewed journals?
A. That is correct.
Q. Have you ever published anything on drug labelling?
A. No.
Q. Are you in the process of writing any articles as we sit here today on drug labelling?
A. No, I am not.
Q. Any articles on Viagra?
A. No.
Q. Have you ever published on Viagra?
A. No.
Q. Have you ever published on

nonarteritic NAION?
A. No, I have not..
Q. I call it NAION, I've been told that we are not supposed to do that. But for the deposition it will show up as N-A-I-O-N, but I'll say NAION.
1974 to 1977 you were at the University of Pennsylvania, urology. What did you do there at that point?
A. Well, kind of to explain. The postgraduate training in urology at the University of Pennsylvania involved six years of training. So the first two years involves basic training of general surgery and gynecology and medicine, to get one ready for your urology training. And at the University of Pennsylvania, it was required that you spend a year in the lab doing research. That's when I spent a year in the lab doing renal physiology research.
And then there is three years of actual urology training. So those are parcelled out perhaps on my CV resume there. I think, it may be confusing. But it's sort

of one period of time that I spent in Philadelphia at the University of Pennsylvania.

Q. How did you like Philadelphia?

A. I liked Philadelphia.

Q. That's where I'm from.

Under the next heading it says "related experience and skills," it says under first bullet, "member of office of new drugs, OND, senior management team, attended weekly briefing in which all important issues across all drug areas are discussed."

To the best of your recollection, was Viagra ever discussed during these meetings?

MS. LESKIN: I'm going to object. Dr. Shames is here -- I will wait for him to come back.

(Discussion off the record..)

(Record read as requested.)

MS. LESKIN: The objection is, and it may be that particular question, I just want to make sure where we are here. Dr. Shames is being offered as an

expert, and he's not here as a fact witness. And there are restrictions on his ability to testify as a fact witness under the terms of regulations that he's been told when he left the agency. So --

MR. BORG: This is when he was at the FDA?

MS. LESKIN: Yes. And the question was was Viagra discussed at these weekly meetings when he was at FDA. I think that particular question is general enough that it can be answered yes or no.

MR. BORG: That's why I'm going to overrule the objection to that. Let's see what the answer is, then we'll -- you can answer the question.

A. I might have to give a little background. That I was on that group toward the end -- in the last two years that I was there. Viagra may have been discussed, I'm not sure. It was in the last two years. It's possible it was discussed. I don't remember.

It's possible it was discussed at that meeting.

Q. Generally what is discussed in these meetings?

A. Generally what is discussed is all the senior management people are there in the various areas of drug development. And the individuals discuss what the important issues are that week or the coming week or past week. And the head of the office of new drugs, Dr. Jenkins, is there. And so everybody at that meeting is kind of aware of what the large issues are.

Q. And you said you would have been attending these meetings in the last two years that you were at the FDA?

A. Correct.

Q. So roughly in the 2006 to 2008 time frame?

A. Yes.

Q. Were issues discussed regarding labelling of drugs that have been approved in the past at these meetings?

A. Probably.

Q. From what I understand you don't remember specifically whether Viagra was discussed during the time frame that you attended these meetings; is that what you testified to?

A. That is correct.

Q. Now, from what I understand, you dealt with the media?

A. Yes.

Q. For the FDA, during what time frame that you were there?

A. Primarily -- well, as a division director, and in the office -- primarily I would say when I was the director of D-R-U-P, DRUP. Primarily at that time. I dealt with media.

Q. I did see in looking at some things in getting ready for this deposition that you did some media for the Ortho Evra birth control patch. Do you remember doing that?

A. Yes, I do.

Q. Did you ever do any media interviews on the issue of Viagra? Or press

conferences, in addition to interviews.
A. I don't recall that.
Q. During your tenure at the FDA, did you ever work on the drug Viagra?
A. Yes, I did.
Q. What did you do when you were at the FDA in terms specifically to Viagra?
MS. LESKIN: Objection. He's not, again, he is not here as a fact witness. And there are restrictions on his ability to testify about facts learned during the course of his employment at FDA.
MR. BORG: What do you have to say about that?
MR. GOMEZ: Judge, he gives a lot of opinions in his report on the labelling, the interactions between Pfizer and the FDA. Maybe I should just focus my question to that.
MR. BORG: Why don't you do that.
Q. Dr. Shames, when you were at the FDA, as you know in this case one of the issues is regarding the labelling of Viagra in

terms of NAION. When you were there, did you ever participate, in your capacity, whatever it was, on that issue?
MS. LESKIN: Objection. Again, his report is based on documents that he's reviewed, and you can ask him specifically what his opinions in the report are based on. But there are ethical and restrictions that he has been given that he's been told that he is not allowed to testify as to facts learned in the course of his employment. And we are not offering him for that basis.
MR. BORG: Well, is your objection a privileged objection?
MS. LESKIN: Yes, on behalf I guess of the FDA, the FDA has instructed him not to provide testimony about facts learned. And I have information he was given when he left, and we can mark this as an exhibit, a summary of post-employment restrictions. And one of the things he was told is former

employees cannot provide testimony concerning information acquired during the course of their official duties.
So you could ask him what his report is based on, and he can tell you what it's based on. But it's not based on his role within the FDA.
MR. BORG: That sounds fair enough.
MR. GOMEZ: I don't want to get the doctor in trouble.
MR. BORG: I know you don't. Part of this is getting educated as to what he is able to do under his obligations.
MR. GOMEZ: Let me ask one more question.
Q. Doctor, please don't answer it until your -- Ms. Leskin has had a chance to object.
During your time frame at the FDA, did you ever discuss Viagra and its adverse events or labelling with any representatives from Pfizer, whether it be through correspondence, email, any sort of

communication?
MS. LESKIN: Are you just asking him did he discuss and not what was discussed? Correct?
MR. GOMEZ: At this point, yes.
MS. LESKIN: So that's a yes/no question that I think you can answer.
A. Yes.
Q. Who did you talk to?
A. Well --
MS. LESKIN: Again, he is just asking the identification.
A. Actually in reality I'm not sure I can remember. There were many meetings, I can't remember the names of the people. The regulatory people at Pfizer. I mean, if you, perhaps if you had those names I might remember. But there were, over the years there were different regulatory people. And the main interactions were years ago. So I don't remember the specific names.
Q. Let me ask this: Yes or no, did you discuss with any representatives from Pfizer the issue of NAION?

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MS. LESKIN: Again, that could be answered yes or no.

A. I'm trying to think. But there were obviously there were written communications.

Q. And those would be reflected in Pfizer's internal documents and in the FDA's documents on Viagra?

A. If you're talking about written communications, then yes. I mean, that counts as -- yeah. Yes.

Q. And if I wanted to look at those I could go find those and look at them?

A. Yes. Well, you have most of them. Right.

Q. Besides correspondence, any conversations with representatives from Pfizer, yes or no, on the issue of Viagra and NAION?

A. I believe there were T-cons, telephone conversations in which I participated. I cannot recall if I specifically said anything, but I may have. So probably. There were T-cons where I was

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there and Pfizer people were there. And so maybe. Or possibly.

Q. Okay. Let me ask you this: When was the first T-con meeting, teleconference meeting you had with Pfizer on the issue of NAION and Viagra? Just when was it.

A. I don't believe -- let me think. I don't believe there were any communications before 2005.

Q. There were no communications where you were involved, or -- is that your testimony?

A. Yes.

Q. Okay. How many teleconferences did you participate in with representatives from Pfizer regarding Viagra and NAION?

A. I can't recall how many. I believe that the information I reviewed correctly reflected the T-cons that were involved. But the information that's available.

Q. We will get into that in more detail later. Are you specifically referring, for example, to the T-cons that took place

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after 2005 on the issue of whether or not a pharmacoepidemiological study should be performed, were you participating in those calls?

A. Some of them, yes. Some. I don't think I -- I think I may have participated in some of them.

Q. Did you indicate if your expert report whether you participated in those calls?

A. In my expert report?

Q. Yes. There is a section on that very timeline. There are telephone conferences mentioned. Did you mention in your report, and we'll get to it in a moment, but did you ever mention that you had been on those calls?

A. I don't think I mentioned in my report whether I did or didn't.

Q. But you're testifying now that you were on those calls; correct?

A. I'm testifying that from the documents that I reviewed and the list of people involved in some of those T-cons, my

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name was there.

Q. Okay. Do you have any independent recollection of -- strike that.

In authoring your report, did you base any of your opinions on what you remember was said during those telephone conferences, or do you base it upon documents that you reviewed that summarized those telephone conferences? Do you understand my question?

A. Yes. I base it on those documents.

Q. Okay. Besides that timeline, 2005 through 2008, on the issue of the studies, do you remember any other specific issues that you talked about with Pfizer regarding Viagra and NAION?

MS. LESKIN: Objection. I think that goes to information he learned during the course of his employment.

MR. BORG: I'll sustain that.

MR. GOMEZ: Okay.

Q. Let me ask it this way, I'm not going to ask you what was discussed, but were there other issues that you discussed with

Pfizer regarding Viagra and NAION?
A. Besides --
Q. Besides the feasibility of a study and the FDA's request to do that, that you discuss in your report, are there any other issues?
MS. LESKIN: That's a yes/no question.
Q. Quantify it numerically, yes or no and then how many.
A. May I rephrase your question or can you? Were there other issues beside the study issue, the observational study issue, the epidemiologic study issue, yes.
Q.. Okay. How many other different issues? Again, I'm not asking what they are, just how many were there.
A. Maybe one other issue.
Q. And you first went to work for the FDA in what year, 1996?
A. Correct.
Q. Were you involved in any way with the approval process of Viagra? And Viagra was approved in 1998; correct?

MS. LESKIN: Again, that's a yes or no question?
MR. GOMEZ: Yes.
Q. Yes or no, were you involved with the approval process of Viagra?
A. Can you define approval process?
Q. Why don't you tell me, what goes into --
A. Let me say this, and then answer that. The drug was not approved in the division which I resided. It was approved in a different division. The answer is yes.
MS. LESKIN: Do you remember the question?
MR. GOMEZ: Yes, I think I do.
Q. Why don't you tell, for a layperson, what's the first step in having a drug approved?
A.. The first step in having a drug approved is getting permission to test the drug in human beings.
Q. Okay. And eventually the drug is approved by the FDA; correct? After numerous other things happen. I don't want to get into

detail right now because I'll ask you about it in your report. Correct?
A. Or not.
Q. Okay. Absolutely.
And Viagra was approved for use in 1998; correct?
A. That is correct.
Q. Now, to go back to the question that you asked me that I asked you that I didn't understand, were you involved with the, yes or no, were you involved with any of the safety aspects of the approval process for Viagra?
A. No. We're talking about the original, we're talking about what the initial NDA approval?
Q. Yes.
A. The answer is no.
Q. What about any of -- let me give a time frame. 1998 to 2001, any post-marketing safety issues, were you involved with evaluating that, yes or no?
A. I can't really recall that, honestly. Was I involved in that? Between

what years did you say?
Q. 1999 to 2001.
A. Now it's '99 to 2001? Yes, the answer is yes.
Q. Same question for the time frame up, 2001 to 2005?
A. Yes.
Q. Were you --
A. Involved, yes.
Q. In what capacity were you involved?
A. Well, for much of that I was -- for much of that I was the supervisor or the director of that division. So I had general supervisory responsibility, authority and knowledge about safety issues.
Q. When you were head of that division regarding safety issues at the FDA, how many people worked under you?
A. My direct reports were 40 or 50.
Q. 40 or 50 individuals?
A. Directly. Let me explain that. The FDA is sort of a matrix organization. So the divisions, the drug divisions have the

medical officers and the toxicologists and certain other people. But there are other people, clinical pharmacologists, statisticians, safety people, who are not directly under the supervision of the director. However, the director supervises the projects that the teams that they're involved with.

So it's sort of direct responsibility, 40 or 50, and indirect responsibility for a lot more for projects involving a lot more people.

Q. You mentioned in your report, I'll ask you more detail later, but you talked about there was a team of people involved with the Viagra, in terms of monitoring for safety issues. How many individuals worked on Viagra specifically?

A. A lot of people at one time worked on Viagra.

Q. Maybe I could --

A. Ten, fifteen. People who worked on it at one time, ten or fifteen or twenty. Viagra was, and maybe perhaps still is, a very

high profile drug. There was a lot of publicity about it. There was a lot of publicity when it was approved. There were a lot of safety issues in the public eye when it was approved. So it required a lot of attention. And person power.

Q. Define for me a high profile drug. What is that?

A. A drug that -- well, there are a lot of reasons a drug can be high profile. Say tremendous use, high media attention, a question regarding safety that may be particularly examined in the media.

Q. Let me stop you there. What safety issues were associated with Viagra when it first came on the market in 1998?

MS. LESKIN: Are you asking him from his role in the FDA or his role public and generally?

MR. GOMEZ: Public and generally.

A. Generally?

Q. Yes. Based on any documents you reviewed.

A. Based on documents that I

reviewed, and my knowledge, general knowledge, there were initially a lot of concern about cardiac issues and interactions between Viagra and cardiac drugs. Those were big, I think, initial issues, big burst of issues.

Q. Okay.

MS. LESKIN: Can we take five minutes, we have been going about an hour.

MR. BORG: Okay, five.

(A recess was taken.)

MR. BORG: Mr. Gomez, your last question? Tell me everything you said. I think Ms. Leskin wants to put something on the record.

MS. LESKIN: We are going to mark a document from the Department of Health and Human Services Office of the General Council Ethics Division entitled "Summary Of Post Employment Restrictions January 2008" that we referred to earlier provided some restrictions on Dr. Shames's ability to provide fact testimony in this case.

(Document titled "Summary of Health and Human Services Office of the General Council Ethics Division, January 2008" marked Shames Exhibit 5 for identification.)

MR. BORG: Okay.

CONTINUED EXAMINATION BY MR. GOMEZ:

Q Doctor, I am going to start asking you some questions about your expert report, and I premarked this as Exhibit 2 and contained within your expert report is also a copy of your CV that is not as current and up to date as the one we talked about earlier, correct?

A Can I check that?

Q I think the only difference is it doesn't mention your current company.

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(Expert report marked Shames Exhibit 2 for identification.)
A Right. That should be correct, yes. Yes.
MR. GOMEZ: Okay. Do you need a copy?
MS. LESKIN: I do. Do you have one? Oh, wait, I have one.
BY MR. GOMEZ:
Q Now, Doctor, you authorized this report?
A Yes, I did.
Q Did you write it yourself?
A Yes, I did.
Q How many drafts of this report did you have before it was finalized?
A It was a -- define drafts.
Q Sure.
When you first started writing the report, I assume there came a time when you finished and forwarded it to Ms. Leskin in written form. Did you ever do that and then make any changes?
A I did not make any drafts and forward them to Ms. Leskin. The process, I did not do that.
Q I am not trying to imply there is

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anything wrong in doing that, I just want to know besides the one I have here today that was produced to us, are there any other written versions of this report that you have on your computer or in your possession?
A No. I -- it was an iterative process.
Q Besides Ms. Leskin, are there any other attorneys at Kaye Scholer, any other attorneys for Pfizer that you sat down and met with in person prior to writing your report?
A I can't tell you the exact time. There were other attorneys that I have met with here during the course of this process, Mr. Spatz and Ms. Hogan. And at one point I met with Ms. Leskin and another attorney in Washington, I believe Mr. Hoffman. I think I had written my report essentially by that time.
Q I saw an e-mail from Ms. Leskin to you. It might have been the first e-mail that mentions that she got your name from Mr. Hoffman. Do you remember that e-mail?
A I think I remember the e-mail, yes.
Q How did you know Mr. Hoffman?
A I didn't know Mr. Hoffman. I was -- I think -- I believe what happened is Mr. Hoffman

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had been working on some litigation with some colleagues of mine, colleagues meaning former FDA people who were working in this area, who were working on certain cases, and I think Mr. Hoffman knew some of them and might have said -- basically I think Mr. Hoffman got my name through somebody else and referred me to Ms. Leskin. I believe that is what happened. I never met Mr. Hoffman previously.
Q Okay. I assume there was an initial meeting that you sat down and met with the attorneys for Pfizer. Do you remember when that was?
A I don't remember exactly when it was.
Q How many meetings did you have face-to-face leading up to the authorship of your report with the attorneys from Pfizer?
A I don't think I had many meetings before the authorship, one or two. I haven't had that many meetings altogether. One or two, I can't recall.
Q I was provided before the deposition, and you also reference in your report the materials that you reviewed regarding your report. Who provided you with those materials?

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A They were primarily provided to me by Ms. Leskin, her law firm.
Q How were they sent to you?
A Federal Express.
Q Was there a cover letter with them?
A There probably was. I don't recall it was.
Q If there was, would that be in your file?
A It should be.
Q I might have missed it because --
A I think there are some in there. There are some letters. Everything -- everything -- you should have everything.
Q Okay. I might have missed it. I did not see any cover letter in the documents that I reviewed --
A Okay.
Q -- prior to today. If you could just check your files to see if there is one.
A Okay.
Q And if there is one, could you provide it to us?
MS. LESKIN: Follow it up with a letter.
MR. GOMEZ: Sure.

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BY MR. GOMEZ:
Q You said a portion of the documents or materials that you reviewed that helped you author your report were provided by attorneys for Pfizer. What specific documents did you go get on your own that helped you write your report?
A I think I looked -- I primarily looked at some websites, looked at the FDA website as some background -- for some background material. I can't recall, for example, the pharmacovigliance guidance and some of the other guidances may have been provided to me, but I also went to the FDA website to look at them and I went to the GAO website --
Q I am sorry, what is that?
A General Accountability Office regarding the report, the report regarding the function of the FDA. And I went to the Institute of Medicine websites because they had a report on the FDA.
Q Any documents that you got from these websites that you relied on in forming your opinions, they would have been cited in your report, correct?
A I didn't cite -- well, I think -- I think we cited the GAO and the Institute of

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Medicine Report, I think, but I know we have said that I looked at those websites. I sent e-mails asking what -- you have e-mails that say that I cited those reports, those websites.
Q Did you ever speak to anybody at the FDA, have any conversations or written communications regarding your opinions that are in your expert report?
A No.
MS. LESKIN: Since leaving?
Q Since leaving the FDA?
A No, I did not.
Q Now, you did not review any of the medical records of the plaintiffs in this case, correct?
A No, I did not.
Q And we went over the depositions that you reviewed, correct?
A Yes, that is correct.
Q Previously?
A (No response).
Q I want to go to your report and start talking about your opinions.
On Page 2 of your expert report is a section titled "Your Qualifications of Expert

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Writing this Report," and rather than go into those, I will pass over those, we went over those in your CV, correct?
A Yes.
Q Okay. Then Section 1.1 is entitled "The following list of items was reviewed in preparation for this expert report."
Going down to the last bullet, it says "Information and experience accrued by myself from my career at the FDA and OND evaluating and supervising the Office of the Safety and Efficacy of Drugs during their entire life cycle from preclinical to post marketing."
What other drugs are you talking about there? Would Viagra -- I am sorry.
A Okay. What other drugs? Well, to start, I was the director of this reproductive and urologic drugs, so I -- at the time, I had experience with drugs that were used primarily by urologists and gynecologists, but I -- you know, lots of drugs, some of which I can mention, some of which I can't. A lot of contraceptives, drugs for reproductive technology, some drugs for prostate cancer, drugs for incontinence, drugs for menopausal -- treatments for menopausal symptoms

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and sexual dysfunction, other -- those -- those -- most a lot of these are drugs that are still under development, but those are the kind of drugs that I had experience with.
Q On Page 4 of your report, you said that the two major organizations within the FDA that are pertinent to your expert report are the Center for Drug Evaluation and Research. I am sorry, within that, the Center for Drug Evaluation and Research, two offices which are pertinent to your report, the Office for New Drugs, the OND, and the Office of Surveillance and Epidemiology, the OSE. Do you see that?
A Yes.
Q The OSE was previously named the Office Of Drug Safety, correct?
A That is correct.
Q Which of these did you work in? Which office?
A Office of New Drugs.
Q Now, what is the difference between the two, the Office of New Drugs and the Office of Surveillance and Epidemiology?
A Well, the Office of New Drugs is the organization that has primary responsibility for

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overseeing the development of the drugs for sure.
Q Okay. That would be, for example, the development of the drugs which would lead up to an end date of approval; is that a fair statement?
A No. It was at least that, but it was more than that. They also had responsibility in post marketing, and they had responsibility to evaluate safety.
Q Okay.
A The other, the Office of Safety, or SA, had primary responsibility -- their total focus was on evaluating safety, technical aspects of accumulating the information and looking at the information, but there was a dual responsibility . in these two offices.
Q Okay. While you were working at OND, were you involved in any of the safety and post marketing issues?
MS. LESKIN: Generally?
MR. GOMEZ: Generally, yes.
A Generally, yes.
Q On that topic, you write in the last paragraph, it says, "Once the product is marketed OND, it has the responsibility regarding the oversight of the continued safety of the drug in

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the marketplace." Did I read that correctly?
A Yes.
Q Okay. And then the responsibility for the oversight of safety in the post marketing period is shared equally with OSE, correct?
A Correct.
Q Turning to Page 5, you write that "After a drug is approved and marketed, staff at OSE and OND gather information regarding safety as the drug is used in the marketplace. This process is called pharmacovigilance."
Can you define for me what pharmacovigilance is?
A Saving and data gathering activities related to the collection, assessment and understanding of adverse events.
Q I think I asked this earlier, and I am going to come back. We will talk a little bit about safety signals. I am going to show you another document, so I am not going to be repetitive because I want to move along, but going down to the middle paragraph, I think it is the second full paragraph, it says "Staff at OND and OSE who have responsibility for Viagra are continuously monitoring adverse events."

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A Excuse me, what paragraph are we on?
Q I am sorry. On Page 5, the one that begins "The main sources," which would be the second full paragraph.
A Yes.
Q I will repeat, "Staff at OND and OSE who have responsibility for Viagra are continuously monitoring adverse events."
How are they doing that? How do they continuously monitor adverse events?
A Well, there is a -- there is a system called the Adverse Events Reporting System in which events are sent to the FDA from various sources, often drug companies or from other sources. They get inputted into this system, they get analyzed. Well, they get coded and put into the system, and various people have access to this system, both the safety people and many times even the new drug people.
And they are looking at -- you know, they are assigned to certain drugs, the safety people are, and so are the new drug people, and they are looking for what kinds of adverse events accumulate in this database, and they are also looking at -- besides the adverse events, they are

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looking at their -- they are looking around for literature reports or other reports that might bear on the safety of a particular drug.
Q Okay. So, for example, if there is a report of a serious condition in a medical journal, is that considered an adverse event?
A It is.
Q Even though it is not reported by the drug company?
A It is considered something to look at in determining if there are safety issues, yes.
Q And I believe --
A Ultimately, usually, those are, in fact, sent in. Those -- those are reported. They --
Q They could be reported from more than one source?
A Yes.
Q And the reporting of these adverse events and any responsibilities to follow up are governed by CFR 314.80, correct?
A Yes -- in post marketing?
Q Yes..
A I believe it is, yes.
Q I will show you that a little later. I want to get into that, but I want to move along

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now.
If there is adverse event in a study, for example, a report of NAION in a study, all caps, does a drug company have a responsibility to investigate that in one of their studies, for example, if it comes from a physician?
MS. LESKIN: Objection, vague.
MR. BORG: I am sorry, the objection is what?
MS. LESKIN: It is a form objection, it is vague.
MR. BORG: Do you understand the question?
THE WITNESS: No, not exactly.
Q I will repeat.
If the FDA receives a report of adverse event from a physician, for example, what do they do with that? Do they inform the drug company?
A I believe if they -- yes. I think they usually try to inform the drug company about adverse events that they receive independently. That is my understanding. It may not be a continuous process, but I believe that is how it works.
Q If an adverse event is reported in a

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medical article, does the drug company have an obligation to investigate that?
A As much as possible.
Q What do you mean by as much as possible?
A They may not have access to the information directly as opposed to when they get information from a physician, say, access in terms of who the patients are, can they talk to the patients, but the drug company will make whatever -- some kind of good faith effort. They are supposed to make some kind of good faith effort to investigate whatever adverse events come to them by whatever route.
Q When you say supposed to make a good faith effort, under what authority?
A The CFR.
Q What authority binds them to do that to make a good faith effort?
A I think the CFR 314.
Q Okay. It is the responsibility of the drug company to investigate adverse events, not the FDA, correct?
A That is not correct.
Q Why not?
A Because I think the FDA does have a

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responsibility to investigate adverse events as well as the drug company.
Q Who would be better equipped to investigate adverse events, the FDA or the sponsored drug company, in your opinion?
A It depends on the circumstances.
Q What circumstances? Give me an example.
A The FDA has -- I think they are both well equipped to investigate adverse events. Both are well equipped.
Q Equally equipped, is that -- I mean, when you say they are both well equipped, I am assuming you mean equally?
A The FDA -- I have to answer -- that would have to be answered in a specific circumstance, but they are both well equipped to investigate adverse events, and they are both charged -- well, both charged with investigating adverse events. The CDER mission statement says that we are providing save and effect -- we have the responsibility to provide save and effective drugs to the public, and the entire time I was there, safety was an important priority.
Q Let me do a little housekeeping on this expert report. I want to point your attention

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before I go back and ask some more specific questions to your Section 5, "Summary and Conclusions."
Could you go there. I think it is on Page 16.
A Right.
Q Okay. Let me go down to under 5.2, "Conclusions." You write, "Erectile dysfunction is a serious condition usually caused by underlying organic disease which causes great distress among men and their partners, often with grave consequences to relationships." Viagra, an extremely effective therapy for ED, is used by tens of millions of patients in the United States."
Is that one of your opinions in this case?
A One of my --
Q Yes?
A This paragraph?
Q In your expert report?
A Yes, I agree with that.
Q Okay. What is your basis for this opinion? Go ahead.
A My basis for the opinion that this

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causes great distress and emotional problems, I was a practicing urologist for many years. At that time I was familiar with the literature regarding erectile dysfunction. I was a urologist before that era. Many patients were willing to go through extreme therapy to correct their erectile dysfunction, such as having surgery, such as injecting themselves in their penis in order to have erections.

I spoke many, many times with men and their partners regarding this problem, and it is clear that this caused a lot of distress. It is public information. There have been advisory committees subsequently, public information advisory committees on drugs for erectile dysfunction in which experts stated that they had patients that would rather die literally than not have their erections. So I believe that condition does cause significant distress, and it is a major emotional and psychological issues to lots of patients and their partners.

Q Okay. Turning over to Page 18, you give an opinion that Viagra did an appropriate job in the post marketing period in terms of pharmacovigilance regarding adverse events. That

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is one of your opinions in this case, correct?

A That is correct.

Q Another opinion in this case is "The oversight by the FDA of the post marketing vision safety issues was appropriately rigorous and included active participation of FDA's ophthalmologic expert. This oversight resulted in adequate labeling modifications regarding vision. These included 1998 changes based on Pfizer's clinical pharmacology trials examining vision effects and reviewed by FDA's Chief of Ophthalmology and a 2005 labeling based on the accrual of Pfizer adverse events and requested by the FDA as a prior approval supplements."

That is another one of your opinions in this case, correct?

A Correct.

Q Another one of your opinions in this case, and I read from your report on Page 18, regarding the interactions between the FDA and Pfizer pertaining to the discussions regarding labeling and observational trials, "I believe these interactions were appropriate and the time frames were consistent for these types of activities."

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That is another one of your opinions, correct?

A That is correct.

Q Going back to Page 17, one of your opinions in this case that "The initial approved labeling for Viagra was found to be adequate by the FDA. The FDA will reject the entire application for approval if the labeling is deemed false or misleading. The sponsor conducted insufficient testing or the risk of therapy outweighs the benefits."

So one of your opinions in this case is the initial approved labeling for Viagra was adequate, correct?

A That is correct.

Q Okay. And that another one of your opinions is that the data submitted to the FDA for initial approval of Viagra by Pfizer and the evaluation of that material by FDA reviewers met the standards regarding safety, efficacy and appropriate risk benefit assessments to allow marketing of Viagra in the United States?" That is another one of your opinions in this case, correct?

A That is correct.

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Q Doctor, we know in July of 2005, the label for Viagra was changed to reflect in a broad sense NAION, correct?

A Yes.. July 2005.

Q We can agree on that?

A Yes.

Q One of the sections where the label was changed was the section under precautions. I think it is under the precautions of patient information?

A That is correct.

Q What is the standard under the regulation that you cite in your report to change the precaution section of a pharmaceutical label?

A The standard for that particular section at that time was that the adverse event was reasonably associated with the use of the drug.

Q Okay. In July of 2005, the change of the label to the precaution section indicates that there was a reasonable association between Viagra and NAION, correct?

A Correct.

Q What is the standard to change the warning section of a label in July of 2005 based upon the regulations that you reviewed?

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A You know, I don't know if I know, but I would -- I believe warnings would require something like it might involve some causation issue. I don't know what they were before. I know currently a warning would require some reasonable evidence of, I think, causation. Let's see, reasonable evidence of a causal association, that is the current standard.

Q Okay.. Going back to the pharmacovigilance.

A Yes.

Q You defined that earlier. What is a signal?

A A signal, a safety signal?

Q Yes. What is a safety signal?

A A safety signal is a concern that that adverse event might occur more frequently than would be expected in a particular population.

Q Okay. Generally, if there is a signal, what is the responsibility of the drug company at that point?

A To investigate the information if they -- if -- to investigate.

Q Okay. To investigate a drug company on their own conduct, a pharmacoepidemiological

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study, correct, generally, to determine if there is some sort of relationship that would require changing the label; is that a fair statement?

A You don't need -- I don't quite understand.

Q Sure.

A You don't need a -- what do you need to change a label? You don't need a pharmacoepidemiological study to change a label.

Q That is not my question. If there is a safety signal --

A Yes.

Q -- do you agree with me that on their own, a drug company can conduct a pharmacoepidemiological study to further investigate?

A Well, I don't think they would do that. There are other ways of looking at a safety signal.

Q I understand that. But my question is: They could on their own conduct a pharmacoepidemiological study to further investigate, that is one of the things that they could do, correct?

A They could do that.

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Q They could do a survey, that is another thing a drug company could do, correct?

A They could do these things, but I do not believe that they would do these things unless they evaluated the safety signal in other more pertinent ways, which are, for example, a safety signal. They would -- a safety signal, someone might be concerned because there were a series of events, good events and good cases.

I believe the first thing they would do before they did a pharmacoepidemiological study, which is a big deal, or any other thing, they would try to assess whether there was -- put things in context, for example. Put things in context to determine whether they thought there needed to be further investigation, how strong is the signal, there are weak signals and strong signals, how strong is a signal.

They also might investigate second things like biological plausibility. They might do mechanistic studies before they went ahead doing a large pharmacoepidemiological study. They could do animal studies. They would do a lot of things before they would move on to do an epidemiological study.

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Q Okay. In this case, we had a change to the precautions section of the Viagra label in July 2005, correct?

A Correct.

Q Yes.

Subsequent to that, and you talk about this in your report in a lot of detail, the FDA contacted Pfizer about doing a study on this issue of Viagra and NAION, correct?

A That's correct.

Q Okay. Would you agree with me that the reason the FDA asked Pfizer to do this study after the change to the label is for safety issues?

A Well, for safety issues. They asked them to investigate to further investigate the safety issue, correct.

Q Because they want to know if there is a safety issue, correct?

A Yes.

Q In your opinion, was there a signal, a safety signal regarding NAION and Viagra?

MS. LESKIN: Is there a specific time?

A When are we talking about?

Q When do you think there was a safety signal regarding Viagra and NAION?

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A I think that from the information that I have read, you know, all of this information, I think certainly by -- I believe there was a weak signal by February 2005.
Q When you say there was a weak signal by February 2005, what did you review specifically? What did you review to form the basis of that opinion?
A I reviewed all of the PSURs, among other things.
Q I am sorry to interrupt you. For the layperson, what is a PSUR?
A Periodic Safety Update Report.
Q Okay.
A These are reports in which a sponsor evaluates all of the safety issues either quarterly or twice a year, depending upon the situation. I reviewed those reports, I reviewed additional reports that Pfizer generated, kind of summary reports regarding safety. I reviewed Pfizer's reports that were sent to the FDA in response to FDA's inquiries regarding the label regarding the information that they had about their clinical trials, information regarding their animal studies, information regarding kind of

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mechanistic studies that they did in human beings regarding the biological plausibility of Viagra being related to NAION. So there's lots of information studies, other outside studies that were done, papers, a lot of information regarding the relationship between NAION and Viagra.
Q Okay. The date of February 24th, 2005, when you mention that date, you are referring to a request by DRUP requested in a letter received by Pfizer on March 16th, 2005, that changes be made to the post marketing adverse events section of the Viagra labeling?
A Correct.
Q You write on February 24th, 2005, "After reviewing the recent data from post marketing adverse events." What specific recent data are you referring to?
A I can't answer what specific data. That wording comes from the letter. The letter that DRUP sent to Pfizer states that we are asking you to put this on the label based on information. I can surmise from my general knowledge and from other information that they were evaluating this safety signal with various data, MedWatch reports, and literature and things like that.

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Q For example, I think you refer to them in the documents that you reviewed of Dr. Pomerantz's abstract in October 2000 of two cases of NAION at that point, correct?
A That is correct.
Q And you would agree with me that NAION is a serious condition?
A We can debate that, yes. From a regulatory sense, it is not totally clear, but you could say certainly from the patient's point of view, it is serious.
Q From a?
A Regulatory.
Q What about from a pharmaceutical company's perspective, is it a serious condition?
A Certainly Pfizer took it as a serious condition.
Q Could you point to anything that you reviewed or anything that you saw that showed Pfizer investigated those two reports in 2000?
A I think when they became aware -- I can't remember. I reviewed all of these PSURs, and every report that they were aware of, they investigated, and it stimulated them to do additional studies, mechanistic studies to see

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whether they thought there was a relationship between -- that Viagra was affecting the blood flow.
NAION is, of course, a condition which is supposed to be related to ischemia of the optic nerve, so one of the key biological issues here is does Viagra cause ischemia, or does it promote ischemia, whatever, of the optic nerve, and Pfizer was very aggressive in pursuing that avenue.
Q Let me back up. I think you just said subsequent to this, Dr. Pomerantz's abstract, that Pfizer conducted mechanistic studies to investigate this issue?
A Yes.
Q Which studies?
A There were -- let me say there were studies done previously to look at the --
Q But that wasn't my question.
MS. LESKIN: Let him finish his answer.
Q Fair enough, Doctor.
A There were studies done previously during the approval process regarding retinal toxicity in humans and animals.
Q You talked about this?
A Then there were studies done afterwards.

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I think some of these studies were done in Stanford, I think, or Penn, excuse me. Actually, Dr. Grunwald did some studies looking, and others did studies among other things looking at the blood flow to the various areas of the retina or the optic nerve to assess that situation.

Q I am sorry, are you finished with your answer?

A Yes.

Q You just testified, and I asked you to follow up on that, subsequent to October 2000, when Dr. Pomerantz's abstract came out citing the two cases of NAION, you said Pfizer did mechanistic studies after that. Which studies are you referring to.

MS. LESKIN: Objection, asked and answered.

MR. GOMEZ: I don't think he answered it.

MR. BORG: Overruled.

A I believe -- I may have the dates wrong, but I believe that is the mechanistic studies that I am talking about were done after 2000. The ophthalmologic studies.

MR. GOMEZ: Real quick, time?

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MS. LESKIN: 1:01.

Q Let's talk a little bit about where we are now. As we sit here today, March 2009, you write in your report that Pfizer is in the process now of conducting a case control study on this issue with Viagra and NAION, correct?

A No.

Q What is the study?

A It is a case crossover study.

Q Explain. What are they looking for in this case crossover study?

A What they are looking for is to see if the incidence of the adverse of NAION occurs more frequently in people taking PDE5 or Viagra than in the population not taking Viagra.

Q What is the purpose of this study?

A That is the purpose of the study..

Q Okay. When were they first asked to do this study?

A A letter was sent to them regarding doing an observational study in December of 2005.

Q Okay. You are referring to on December 21st, 2005, DRUP sent a regulatory letter to Pfizer in regard to, quote, "rare post marketing reports of vision loss due to NAION in

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men who have taken PDE5 inhibitors, including Viagra"?

A I think that is the letter in which they ask for a -- a post marketing study.

Q In fact, Doctor, they recommended, or they write in the letter that "We recommend that you conduct a case control study of incident NAION cases;" is that correct?

A That is correct.

Q The objective of this study would be "to determine whether use of PDE5 inhibitors is an independent risk factor for NAION," end quote, correct?

A That is correct.

Q The letter went on as you write to recommend certain technical aspects of the study and suggest that Pfizer consult with FDA's," quote "Guidance for industry on good pharmacovigilant practices and pharmacoepidemiology assessment, March 2005," correct?

That is a document that I want to show you before the end. I want to talk about that because you do mention it a few times in your report. What was Pfizer's response to that letter?

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A Pfizer's response was that they provided information in which they said they believed that there was sufficient information to say there was no increased incidence of NAION in patients taking Viagra, and two, they weren't sure a case control study was feasible. They give scientific argument regarding why a case control study was not feasible.

Q Okay. But as we sit here today, they are doing this study?

A No, they are not doing that study.

Q What is the difference?

A The difference is that ultimately, there is a lot of technical interactions between FDA and Pfizer.

Q Okay.

A Ultimately, FDA realized that, in fact, a case control study is not feasible, and then we get into the discussion about a case crossover study. But ultimately, the FDA acquiesced or agreed with Pfizer that a case control study would take too long or, you know, was not feasible in this situation. So then they got into further discussions.

Q The purpose of this case crossover study

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that we are speaking of today --
A Yes.
Q -- is to investigate the relative risk of NAION when patients are exposed to PDE5 inhibitors compared to when they are not?
A That is correct.
Q Okay. If they find that the relative risk -- explain that to a layman. What does that mean, relative risk?
A It means that the chance of getting NAION would be more if you took Viagra than if you had not taken Viagra, if that is what the result of the study shows.
Q And --
A They are looking to see if it is true that the chance of getting NAION is when you take Viagra than when you don't take Viagra.
Q That is information that a prescribing physician would want to know, he would find that helpful in determining whether or not to prescribe a drug to his patient, correct?
A I am not sure about that. The label already puts physicians on notice that there is some possibility that there may be an association, so I really can't answer that question. You would

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have to --
Q I am sorry, Doctor. I didn't mean to interrupt. I told I am bad at that.
If the results of this study show a relative risk that is high in epidemiological standards, that is something that a prescribing physician would want to tell their patient; would you agree with that?
A If -- well, I guess that -- I think that is true if it is -- if it is substantial information.
Q What do you define as substantial information? What would be a relative risk that is substantial? Would you explain that to a layperson?
A It is hard to answer that question. Maybe -- I don't know if I am the right person to answer that question, to tell you the truth. There is a lot of unknowns here about how a physician would react to these things, how physicians take into account labeling, you know, that kind of thing. I am not sure I can answer that question.
Q The purpose of this study that is going on right now is to investigate the relative risk

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of NAION when patients are exposed to a PDE5 inhibitors like Viagra?
A Yes.
Q Compared to people who are not, correct?
MS. LESKIN: Objection, asked and answered.
MR. BORG: Overruled.
Answer it.
A Repeat the question.
Q Sure.
I am going to quote what you write in your report.
MS. LESKIN: What page?
Q Page 16, last paragraph before Section 5.F, you write, "Pfizer acquiesced to the FDA's technical and temporal parameters regarding a case crossover study to investigate the relative risk of NAION when patients are exposed to PDE5 inhibitors compared to when they are not."
As of the writing of this report, Pfizer had begun accrual of patients' details of the study which can be found at clinicaltrials.gov. Assume for purposes of this next question that the results of this study show a statistically significant relative risk of NAION when patients

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are exposed to Viagra or any other PDE5 inhibitor compared to when they are not. If that is the case, is that something a prescribing physician would want to know so they can relay to their patient when prescribing the Viagra?
MS. LESKIN: Objection, improper hypothetical, lack of foundation.
MR. BORG: Overruled.
Are you able to answer that question?
A I disagree with the assumption. I disagree with the assumption because I -- I -- quite frankly, my opinion is that this epidemiologic study is not from -- not going to show any difference because I feel there is enough information to indicate that there is no difference.
Q Okay.
A Or little difference.
Q That's a new opinion. You are now --
A Right.
Q That is not in your report?
A Right.
Q So you are giving an opinion now you don't think the study is going to show a relative risk? You don't think that?

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A I don't think so.
Q Okay. Based on what?
A Based on the information that I have reviewed regarding NAION.. All of this other information regarding the risk, the cases we have here relative to the background information, the mechanistic studies, all of this information together leads me to believe, in my opinion, that we will not find -- there will not be found an increased relative risk of NAION when -- at the completion of this study.
Q If that is the case, why does the FDA want Pfizer to do the study?
A Well, there are people --
Q What is the purpose of the study?
MS. LESKIN: Objection, compound.
MR. BORG: You have two questions. I bet you want them both answered.
BY MR. GOMEZ:
Q As you sit here today, why does the FDA want to do it, then? I will stop there.
A I don't see -- the FDA, from the material that I reviewed, was interested in further studying this event, which is appropriate, and you said to me assuming that the study shows

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an increased risk, and I answered that by saying I don't agree with that assumption. The FDA is doing this because the people at FDA involved here believe that it is appropriate to investigate this issue further. That is why they asked for this study.
Q And you disagree with that?
A My personal opinion is that -- my expert opinion is that this study did not show a difference between Viagra and --
Q Did you convey that in 2005 on any telephone conference?
MS. LESKIN: Objection. It is protected, Exhibit 5.
MR. BORG: When he was working for the FDA?
A I can't answer that question.
MR. BORG: I don't think he can, either. Sustained.
BY MR. GOMEZ:
Q All right. We can agree that there was a safety signal with Viagra and NAION even though you call it weak, correct?
A That is correct, in 2005.
Q Right. There was a label change,

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correct?
A Yes.
Q After 2000, when there were two reports of NAION, I believe there were two reports of NAION associated with Viagra, according to Dr. Pomerantz's abstract. Is that a signal in your opinion?
A In my opinion?
Q Yes.
A I would have to see the specific reports, two reports by themselves. A safety signal is a concern. You have to look at the reports if we are talking about specifically, but in general, you look at the reports, and reports have a lot of difficulties, there is -- they could be duplicate reports, they could be insufficient reports.
So you have to first look at the reports, evaluate the quality of the reports and then accumulate in your ongoing investigation, accumulate a series of reports and then put those series of reports into context regarding the background information, think about biological plausibility, and at some point during that process, someone or a group of people, and usually

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at the FDA, it is a team effort, so at some point, a group of people would decide there is a safety signal, and at that point, there are continuing investigations regarding whether we generally meet the standard of wanting to put something in the label, is there evidence enough to put it in the label or at least discuss with the company to put it in the label.
And the company goes through the same process because companies are going through the same process of looking at safety signals, and investigating and then go further on to determine whether the information should be put on the label.
Q You would agree with this general proposition that one serious adverse event can be a signal?
A Can be generally.
Q Generally?
A Yes, right.
Q Yes?
A But those circumstances, they would have to be -- there are circumstances, for example, when you would have an event that was unheard of in the population, and something occurred which

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normally would never have occurred in the population, and you had a really good case, something like that, which of course, is not at all which we have with NAION, but it is a possibility.

Q You would agree with me that NAION is a serious adverse event?

A In a medical sense, maybe not in a regulatory sense. It is something that is very serious to the individual, absolutely.

Q It causes blindness, correct?

A Sometimes.

Q But it causes blindness?

A Sometimes.

Q Blindness is a permanent condition, correct?

A Sometimes.

Q Obviously I agree with you. Sometimes it can resolve, correct?

A Yes.

Q But we can agree medically serious adverse event, correct?

A Correct.

Q Okay. What did Pfizer do to investigate these two incidents of NAION referenced in

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Pomerantz's 2000 abstract?

A Pfizer, when they received these reports, looked at the reports. When we received the actual reports, looked at the reports, put them in context, put them in the context of all of the other visual events, and at the same time they were looking at all sorts of other events, but they -- from everything I have read, Pfizer was very aggressive about evaluating all of their adverse events, including their visual effects from the information I have.

Q But is there anything to indicate in the record that you have reviewed, please point it out to me, that Pfizer tried to contact these patients?

A I don't recall anything like that.

Q They could have done that if they wanted to, correct?

A They may have done that, I don't know. I don't specifically.

Q Fair enough.

A They are obligated to contact -- according to the regs, they are supposed to try to get more information and do follow-up for these serious adverse events. And there are impediments

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sometimes in terms of things like patient confidentiality. Sometimes the FDA or the company will try to get further information, but they may not be able to get further information, you know.

Q But sometimes adverse events are underreported, correct?

A Estimates?

Q No, strike that.

There is a general rule out there that adverse events are underreported for certain incidents?

A What is better to say is that we don't know whether things are underreported or even overreported. For many drugs, they may be underreported. For a drug like Viagra, they may be overreported. We know that, that is all I will say for now.

Q Going back to this case crossover study.

A Yes.

Q What is the status now as of March 13, 2009, of the study?

A My understanding from the public website is that they are accruing patients. That is all I know about it, they are accumulating patients.

Q Let me ask you this: You would agree

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that Pfizer knew of a possible association between Viagra and NAION in 2000, correct?

A No.

Q Well, they knew of patients who had taken Viagra and had developed NAION in 2000, correct?

A Correct, I think.

Q Why not just do a study then? Why not?

A We have to put things in context. There were two reports. Quite frankly, I don't even know if the two reports were on NAION, but there were two reports of something, some sort of ischemic optic neuropathy, among maybe -- ultimately, when the report in 2005 was made public, it included foreign reports and American reports.

In a particular year, there were perhaps 100 million tablets, at least, maybe 150 million tablets of Viagra administered, taken by people. Among that, there were two, maybe, reports of NAION. They investigated those reports as they investigated all sorts of other reports about all sorts of things that came into them, and something like that didn't rise to the level of a signal or anything. If that standard was appropriate for

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those two cases, they possibly would be doing God knows how many, 50 epidemiology studies. If they had two reports of something, there are two reports of many different things.

Q But, Doctor, they had more than two reports? Prior to July 2005, they had more than two reports?

A That's right.

Q In fact, from January 1998 to December 2004, Viagra was associated with the highest number of ischemic optic neuropathy reports, 19 percent in the AERS database, you would agree with that?

A I have seen that written. I have no --

Q That is something that comes from the 2005 Public Citizen Watch Letter that was sent to the FDA, correct?

A That analysis was in there, yes.

Q And that is what we called data mining?

A Yes.

Q And you state data mining is unreliable, correct?

MS. LESKIN: Objection.

Q In your report, generally?

A It is not just me. Data mining is kind

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of an exploratory analysis that is even at a lower level than the analysis one has from looking at the ARS work report because it is based on the ARS reports. And actually, one of the flaws of that, I think, in Dr. Wolfsen's petition, he compares Viagra and maybe PDE5 inhibitors in general with other drugs, which is specifically cautioned against in the pharmacovigilance guidance.

Aside from the fact that there are particular problems with what he did, there is a general opinion that most people agree that you should not be comparing different classes of drugs in a data mining exercise.

Q We are talking about the Pomerantz report in 2000, he reported the seven additional reports in 2005, correct?

A I think it was 25, yes.

Q Adverse events just don't come from the United States, correct?

A Serious adverse events, yes.

Q Serious adverse events like NAION?

A Correct.

Q Pfizer has an obligation to look around the world, correct?

A Yes.

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Q Do you know about any incidents of NAION being reported in Europe in the time frame of 2003? Did you review anything?

A There are several things I can comment about.

Q Sure.

A One is that there were several observational studies in -- one was in U.K. and one was in Europe after it was approved there, I am not sure of the exact timing, where both in the U.K. study and the European study, the conclusion was that there was no increased incidence of NAION.

The second thing I can comment about that in the final public comment that FDA made in July of 2005, after all of this labeling changes, the FDA broke down on their website where the reports came from, and some of the reports in the analysis were foreign.

So there were both foreign and U.S. reports in the final 2005 analysis, and Pfizer, in fact, was required, I believe by regulatory authorities, to do both of these European studies -- I should say English and European studies. So they were investigating.

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This is just one of the ways that they were investigating foreign reports, and when you read -- one reads the PSURs, you can see these reports broken down by country as well as the number of drugs. It is distribution of the drug by company. So they were analyzing foreign information, also.

Q The February 2005 letter from the FDA from Pfizer regarding changing the labeling, the information that the FDA was relaying to Pfizer that they were basing their request on was something that Pfizer had in their possession, too, correct?

A Not completely. Perhaps.

Q What do you mean by not completely?

A I believe that it is.

Q Are you saying that the FDA had more information than Pfizer?

MS. LESKIN: Wait, one person at a time.

Q I am sorry.

A The FDA often has different information. They most likely had similar adverse event reporting.

The 2005 labeling request, from the information I read, was precipitated by

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accumulating events by Viagra, but perhaps other PDE5 inhibitors which Pfizer probably had no information regarding. This was, in my view, a class -- a request for class labeling because FDA actually says that in a letter, you know, the next letter that they write. So some of the information, I believe, perhaps regarding other drugs was not at Pfizer's disposal.

Q You write specifically that in your report on Page 13, right before 4.4, you said, "I believe that the resultant labeling was adequate, and the time frame for implementing this labeling, considering these changes involved other sponsors in this case, class labeling was appropriate."

What do you know about the other sponsors?

MS. LESKIN: Based upon public information?

Q Based on what you reviewed --

A Okay.

Q -- to write that statement?

A Well, the labeling -- the FDA in their letter, which I have access to here, says that they are going to do class labeling in the second letter, and also in the FDA public statement in

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July, they talk about the other two drugs. They talk about -- it is Viagra, Cialis and Levitra.

Q You would agree with me that Viagra is No. 1 in terms of sales and prescriptions?

A It was at that time.

Q It still is?

A I am not sure. I don't know for sure.

Q In fact, Viagra has been reported in some years as 1.9 billion in sales, correct?

A I don't know.

MR. GOMEZ: What time is it? How much time do we have?

MR. BORG: It is 1:25.

Q Going back to Page 16.

MS. LESKIN: Of the report?

MR. GOMEZ: We are still with the report.

BY MR. GOMEZ:

Q Now, you refer to an August 2nd, 2007 face-to-face meeting between Pfizer and the FDA, correct?

A Yes.

Q Okay. Then you write at that time, "FDA was primarily interested in the time frame to complete the study and was willing to sacrifice

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precision for rapid conduct of the study." Did I read that correctly?

A Yes.

Q So the FDA wanted this study to happen faster than it was, correct?

A Yes.

Q Why?

A I can't tell that exactly from this information.

Q Why would the FDA want to do a case control study?

MS. LESKIN: He was finishing his answer.

MR. GOMEZ: I am sorry, I thought he was done.

MS. LESKIN: You can finish your prior answer.

A Yes, from the information I have been given, everything I have read, I am not sure why they were so anxious. I can understand why they were so anxious to get the thing done and apparently less concerned about the correct conduct of the study. I can't really answer that question.

Q Would it be fair to say that the FDA

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wanted the study done in a rapid manner because there were safety issues at stack?

A I think that the FDA wanted -- clearly the FDA wanted the study accomplished, yes, to further investigate the safety issues.

Q Would you agree with this statement, that if the results of a study showed that there was a safety issue with Viagra, that that would hurt Pfizer's sales of Viagra? Do you agree with that?

MS. LESKIN: Objection.

MR. BORG: Overruled.

A In regard to if there was some -- you know, I am not sure that is true.

Q Okay. You would agree if the FDA wants the study done fast for safety issues, why doesn't Pfizer want to do the same thing?

A Because there is no point doing a study. You are wasting a lot of resources doing a study where the results will be questioned. Epidemiological studies are often questioned. They are very difficult to do, much harder than control studies. Almost every epidemiological study that I have seen, there are questions about all sorts of issues.

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So it is very important to get these parameters correct from the beginning. In this case, from what I have read, Pfizer was making a good faith effort to get everything correct. In fact, they hired one of the main -- one of the main people, the consultant was somebody who the FDA quotes in their pharmacovigilance guidance. They may have made every effort to get all of this information and the conduct correct, and the FDA on its own says, essentially, well, you know, we know there are some problems here, but let's just go ahead and do the study. I cannot answer why that was, but that is clearly shown in the information that I read.

Q We can agree on this, that the study was requested at the end of December, December 21st, 2005, over three years have gone by, and the study is still not completed, correct?

A It is not completed.

Q I guess --

A However, even if they started the study when it was requested, it wouldn't be completed at this date.

Q How long is the study going to take to be completed?

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A Well, that was one of the controversies about this. I don't know the current, but at one point, someone thought it might take 10 or 15 years. I am guessing, I don't have the date. Maybe five or six years, I just don't know. I don't have enough information.

Part of the problem is that a more precise study would have taken a longer period of time. The FDA didn't want to take that long, and they were willing to accept less precision for a shorter study.

Q Well, at first, Pfizer didn't want to do the study at all because they thought it wasn't feasible, correct?

A That is true. And the FDA agreed with them, that a case control study was not feasible. Then they switched to a different kind of study that was perhaps more feasible. The FDA's own ophthalmologist, and it is quoted in the telecon, Dr. Wiley Chambers, stated in one of the -- either in a letter or the telecons that he did not think that the case control study was feasible.

Q On April 12th, 2006, DRUP believed that a prospective case control study was feasible, correct?

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A I think in that same letter, they talk about disagreement, and he didn't -- that there were -- in one of the letters, they talk about disagreements.

Q Right.

A Ultimately, they changed their mind and said let's do a case crossover study rather than a case control because a case control, it would take too many people, and it would take too long. A lot of this discussion was surrounding the type of study to do.

Q "On April 12th, 2006, the division informed Pfizer that in consultation with the division of drug risk and valuation in OSE that 'while many of the design issues for such a study require further discussion, DRUP believes that a prospective case control study is feasible and may provide additional information toward determining the potential risks of PDE5 inhibitors as independent contributors to NAION events.'" Did I read that correctly?

A Yes.

Q Okay. Then you talked about Dr. Chambers?

A Yes..

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Q You write on Page 15, the second to the last paragraph, okay?

A Yes.

Q "In its written response to Pfizer's October 9th, 2006 submission described above, DRUP sent draft comments in preparation for a teleconference to be held between the appropriate FDA and Pfizer clinical and regulatory experts." I will stop right there.

Were you on that conference call; yes or no? That is all I want to know.

A I don't remember. I can easily check the records and see if I was on the conference call.

Q In these comments communicated by DRUP, it was stated there are different opinions within the collaborating groups regarding the feasibility of an epidemiologic study. For example, Dr. Chambers," who you talked about, "and the FDA ophthalmology experts expressed, meaning prospective case control study is not likely to be doable at this time." Did I read that correctly?

A That is correct.

Q And DRUP further stated that although it believed that a prospective case study is

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feasible, it recognizes that the definition of NAION in the exposure window are two areas that need additional discussion. DRUP still believed as of March 23rd, 2007, that a case control study was feasible, correct?

MS. LESKIN: Objection, misstates the evidence, lack of foundation.

MR. BORG: Overruled.

If you are able to answer.

A Restate that question.

Q As of March 23rd, 2007, DRUP believed that a prospective case study was feasible, correct?

A But as I state, there were differences of opinions internally.

Q Fair enough. And we talked about that, right?

A Yes.

Q How many studies did Pfizer do to get Viagra approved?

A Ten human studies, maybe 20, 30, 40 animal studies. Another 50, something like that, just off the top of my head.

Q Have I covered all of your opinions that you are going to give, if asked to testify?

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A (No response).

Q Have I covered all of the ones in your report?

A Covered all my opinions?

Q Yes..

A Yes, we went through the conclusions which are my main opinions.

Q Okay.

A I have lots of opinions.

Q Sure. We could sit here all day and ask you about that, but --

A I have opinions about Dr. Bloom's opinions, which of course, the big issues are covered.

Q The opinions that you will testify to are contained in this report?

A Yes.

Q Are you going to give any other opinions that aren't in this report?

A I don't think so.

Q I guess what I want to ask is: Pfizer conducted over 20 to 40 human studies to get Viagra approved, correct?

A It was efficacy, does the drug work.

Q Does the drug work and is it safe,

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correct?

A Yes.

Q After it is approved in 1998, all the way through July 2005, you would agree with me in between that time frame, whether it be 2000, 2001, 2002, that Pfizer became aware that there were reports out there that a very serious eye condition called NAION was being suffered by people who were taking their drug Viagra. Would you agree with that?

A That they were aware that people were getting NAION who also happened to be taking their drug, that is true.

Q They were aware of reports that were out there?

A Yes.

Q Why not do one more study? Why not?

A Well, I guess I sort of gave that answer before. If you put that standard to it, there were people out there with all sorts of stuff going on. I mean, these were -- these are older men, okay, and they were getting everything that older men get. NAION is one of them. But they -- if you look at the PSUR reports, there are reports of all sorts of serious things going on with these

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older men. So they could have done -- they would end up doing multiple studies using that standard, in my opinion. Every time they got a report about some serious event, not even saying the studies are feasible, we didn't even know if these studies were feasible, doing multiple epidemiological studies, taking up multiple resources, costing a lot of money for the people at the FDA. Forget about Pfizer, people at the FDA do not -- everyone considers the resources involved in doing a study.

So there would be no motivation to just do studies every time one or two events -- reports of a serious adverse event came in when it is not even to the level of a safety signal, much less even to be on the label.

Q But they are doing the study now; aren't they, correct?

A They are doing the study now, that is correct.

Q We have had a label change, correct?

A That is correct.

Q In the precautions section of the label, correct?

A That is correct.

Q The standard for a precautions section

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label change is that there is a reasonable association between the drug and the event, correct?
A Correct.
Q Pfizer never took it upon themselves to change the label, correct?
A Not from the information that I have here, correct.
Q So it is your opinion before we stop, that the label change was timely, correct?
A That is correct.
Q We went over everything that you base your opinion on, it is in your report?
A That is correct.
Q Okay. It is your opinion that the study that was asked to be done in 2005, the case crossover study, is being done in a timely manner, correct?
A In a timely manner, correct. Yes..
MR. GOMEZ: Let me have a second to go through my notes.
MR. BORG: Mr. Gomez, don't rush this because of me.
(Recess taken)
MR. GOMEZ: As Exhibit 3, CFR 314.80.

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(CFR 314.80 marked Shames Exhibit 3 for identification.)
MR. GOMEZ: "Guidance for Industry," I am going to mark this as Shames 4, please.
(Document titled "Guidance for Industry" marked Shames Exhibit 4 for identification.)
BY MR. GOMEZ:
Q Real quick, Page 9 of your report. Are you there?
A Yes.
Q The second full paragraph down, it's one beginning with "ED," there is a sentence in there?
A Yes.
Q That says, "Therefore, it is not possible to say there is a causal relation between NAION and the use of Viagra."
A Correct.
Q Yes?
A That is what I said. Therefore, it is not possible to say there is a causal relation between NAION and the use of Viagra, right.
Q When you say causal relation, define that.
A A causal relationship to my view is when there is a high level of evidence that the drug is

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related to the particular adverse event, the biological event. There is no standard definition of causality by the FDA or anyone else that I know. There is some subjectivity. That is my definition of causality.
Q Just so that I understand you, you talked earlier about changing the precaution section of a label, correct?
A Yes.
Q Okay. We agreed that to put a change in that section, there has to be reasonable evidence of an association, correct, between the drug and the event, you agreed to that?
A Right, whatever reasonable association.
Q So when you say it is not possible to say there was a causal relation between NAION and use of Viagra, you are putting that on a continuum above reasonable association?
A The evidence for causation, I would say, is much higher than reasonable association.
Q Percentage wise, what is it?
A Percentage wise, I don't even know what that means.
Q More likely than not?
A (No response).

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Q What is reasonable evidence of association?
A Reasonable evidence of association in terms -- in practical terms in this situation is when the FDA decides there is a reasonable evidence of an association. That's in reality what it is.
Or in fact, a drug company could look at the regulations and decide when they believe there is a reasonable evidence of association.
Q It seems like you are saying two different things. You are saying there is not a causal relationship, you also testified there is a reasonable evidence of association?
A I may be wrong, but I think causation is a much higher -- causation is much higher, a higher level of -- on a continuum, you have a suspicion, then you have an association, but these are not causation. Causation means the drug -- you know, if you have a drug that causes liver failure, or aplastic anemia or something, and that never occurs in this population given the drug, but if they get aplastic anemia, you can consider that the evidence is much higher, that might be causation. There is nothing here that indicates

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causation. You don't need causation to be on the label.
Q What is your understanding of causation? On the continuum, where is the causation?
A Causation is way out there.
Q Is that 75 percent?
A I don't know how that --
Q More likely than not, is that evidence of causation?
A You know, causation is such a high standard. I don't think it ever appears in the FDA label. To be sure of causation, it is very, very unusual that you would actually kind of be absolutely assured of causation, so --
Q Where would I find that in the documents you reviewed, that definition?
A well, I don't know about the definition of that. In the pharmacovigilance guidance, it says that the FDA has no standard definition of causation, rather it says there is no real good standard of causation.
Q I don't mean to belabor the subject, you say they don't have a standard definition for causation. Correct me if I am wrong, your understanding for causation is way up there, you

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said? I am just trying to understand what is your definition of causation.
A My understanding is you take this drug, you are going to get this, that is my -- that to me is a causation.
Q So in other words, correct me if I am wrong, if you take a drug, and you get a condition, it is the cause of the condition, would that be your definition?
A No, no. I mean, if there is no other reason for you to get this than that, that could be causation. There is no other reason for you to get this, you take the drug and you get it, that might -- and that happens multiple times.
Q So it is your testimony that there can't be more than one cause of an event?
A I didn't say that.
Q Am I understanding you correctly, that is what you are saying?
A No, I didn't say that. I said -- I said the drug could be a cause, but there certainly could be other causes.
Q Okay.
A I mean, you know.
Q Let me go to Page 12 at the top. You

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say, "When the agency or a sponsor seeks to alter safety related labeling." We can agree that the sponsor, Pfizer, didn't seek to alter any safety related labeling in this case, correct?
A I am not aware of any, no.
Q A few things, general propositions I want to ask you about, and then we are done regarding post marketing.
Would you agree with me that once a signal is detected, adverse events should be fully and quickly evaluated to determine if a safety risk is identified? Would you agree with that statement?
A It should be further investigated, correct.
Q Okay. Would you agree with me that a sponsor or a pharmaceutical company is required to review information with the FDA to determine if additional studies are needed to address safety concerns?
A Say that -- at what point is this? Just in general, what do you mean?
Q These are general propositions.
A That a company is required to -- yes, they --

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MS. LESKIN: Can you repeat the question.
Q Would you agree with me that a pharmaceutical company is required to review information with the FDA to determine if additional studies are needed to address safety concerns?
A I don't know if that is an actual requirement. I mean, it is certainly a good idea, I agree with that. I just don't know if there is a regulatory requirement, that is what I am not sure about. Companies sometimes will often do studies that the FDA is not aware of. It might be in Europe or somewhere. Sometimes they might do studies elsewhere or -- I am not sure they need permission, but in most cases, it is a good idea to talk to the FDA, I can agree to that. Whether they are required, I just don't know.
Q You would agree with me that the duty to act quickly and promptly, as we discussed just a moment ago, falls to the manufacturer?
A Quickly and promptly regarding -- I think both the FDA and the manufacturer have a duty to act promptly to investigate safety issues, yes.

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MR. GOMEZ: I think that is all I have. I might have one or two more.
EXAMINATION BY MS. LESKIN:
Q I have a couple of questions to follow up, Doctor.
We talked a little bit today about pharmacovigilance?
A Yes.
Q Mr. Gomez asked you about the number of reports of NAION that existed at various points in time. Is it acceptable pharmacovigilance methodology to similarly count the number of adverse events before taking an action such as changing the label?
A No. The pharmacovigilance guidance specifically says how one should individually evaluate the reports, the individual reports. This evaluation includes information related to the adverse event, like when did the adverse event occur, what is the extent of the adverse event, what are the symptoms and signs of the adverse event, the timing of the adverse event related to the drug, the clinical course of the patient after the adverse event, whether the adverse event did or did not require hospitalization, whether it was

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disabling or not disabling, as much detail as possible how the adverse event was diagnosed, laboratory studies, the diagnostic criteria. A condition like NAION requires, of course, a lot of diagnostic tools to diagnose it.
Q Is the total number of prescriptions being written a relevant factor to evaluate?
A Absolutely. It says -- it specifically states in the pharmacovigilance guidance -- there is a whole section about context that requests people to create reporting rates and compared to background. On its face, of course, it makes sense to have to put this in context, so it is a very important part, and the FDA believes it is an important part.
Q When you say background, is the background rate of the event relevant to proper pharmacovigilance?
A Absolutely. And it is again stated in this guidance, but it only makes sense that it would be important if you have an event that is reported two or three a year, and in one case, this event has never been reported ever in the history of that population. That would make -- it might make you think one thing.

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If, however, it was reported two or three a year, and there were millions and millions of people taking it, and in this population of the people taking it, this event occurred in a defined manner, then you would look at it in some other different way. It would make you evaluate it differently.
Q Would it be appropriate pharmacovigilant methodology to suggest a label simply on a count of the adverse event without doing this analysis that you just described?
A Absolutely not.
Q Mr. Gomez asked you some questions about studies Pfizer had conducted. Following the approval of Viagra, did Pfizer conduct additional studies of the drug?
A Yes.
Q Additional clinical studies?
A Yes.
Q I want to direct you to Page 8 of your report, and there is that third paragraph from the bottom. Are you there? It starts "no cases."
A Yes.
Q How many patients were involved in the original clinical data set that was submitted to

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the FDA in connection with the Viagra NDA?
A The people exposed to Viagra were 3,800, right.
Q Directing you to Page 14 of your report, the paragraph talking about the August 5th, 2005 Pfizer letter at the top of that page. Do you see where I am?
A Right.
Q As of August 5th, 2005, how many patients had participated in clinical trials for Viagra?
A Approximately, 13,000.
Q So that is about --
A 13,000 took Viagra, so that is, you know --
Q It is a little less than 9,000 additional patients were involved in clinical studies between the time of approval and August of 2005; is that fair to say?
A That is correct.
Q Did any of those patients get NAION?
A None of those patients got NAION.
MS. LESKIN: I have nothing further.
CONTINUED EXAMINATION BY MR. GOMEZ:
Q One or two follow-ups on that very

issue.

Doctor, you can agree with me that the studies that Ms. Leskin just referred to weren't designed to look for NAION?

A Generally, they were not.

Q Even though you had all of these studies, you would agree with me that the FDA still wanted an additional study done on this very issue?

A That is true.

Q Okay. So you would agree with me that as a former employee of the FDA, if a study had been done on this issue regarding Viagra and NAION previously, you wouldn't ask the company to do a study again; would you?

MS. LESKIN: I want to make sure of the context you are asking as an expert, not based on what he knew at the time he worked at the FDA, correct? I want to make sure. You said as a former employee.

Q I am asking you as an expert, and part of your expertise is based on your FDA experience, correct?

A The answer is that there would have had to have been a reason to do the study in the first

place.

Q That is not my question, with all due of respect.

A I didn't say you wouldn't do another study. It depends on the record of the first study. The first study might have been equivocal. Just because they did one study on a condition on a situation doesn't mean they wouldn't have asked. I have seen times where they would ask for another study. It depends on the first study. Maybe the first study was equivocal, and then they would ask for another study, or there was criticism of the first study.

MR. GOMEZ: Doctor, that is all I have. I appreciate your time. It was a pleasure.

(Time noted: 2:08 p.m.)

____
DANIEL A. SHAMES, M.D.

Subscribed and sworn to before me this ___ day of ____________, 2009.

____
NOTARY PUBLIC

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I, ANITA SHEMIN, a Certified Shorthand Reporter and Notary Public within and for the State of New York, do hereby certify:

That DANIEL A. SHAMES, M..D., the witness whose deposition is hereinbefore set forth, was duly sworn by me and that such deposition is a true record of the testimony given by the witness.

I further certify that I am not related to any of the parties to this action by blood or marriage, and that I am in no way interested in the outcome of this matter.

IN WITNESS WHEREOF, I have hereunto set my hand this ____ day of ___________, 2009.

____
ANITA T. SHEMIN, CSR

DANIEL A. SHAMES
CERTIFICATE
STATE OF NEW YORK)
: ss.
COUNTY OF NEW YORK)

I, ERIC J. FINZ, a Shorthand Reporter and Notary Public within and for the State of New York, do hereby certify:

That DANIEL A. SHAMES, the witness whose deposition is hereinbefore set forth, was duly sworn by me and that such deposition is a true record of the testimony given by the witness.

I further certify that I am not related to any of the parties to this action by blood or marriage, and that I am in no way interested in the outcome of this matter.

IN WITNESS WHEREOF, I have hereunto set my hand this ____ day of _____, 2009.

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ERIC J. FINZ

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MARCH 13, 2009

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EXHIBITS